The physician may also monitor the plasma ammonia levels and dietary protein intake in the patient to ascertain whether the patient's dietary protein intake and drug treatment combined are producing the appropriate therapeutic effect. Dietary protein intake or drug dosage or both could be adjusted to attain a normal or desired plasma ammonia level, e.g., a level below about 40 umol/L. However, as demonstrated by the observations described herein, the physician would not use plasma levels of PAA or PBA to adjust the dosage of HPN-100 or otherwise guide treatment, as those levels do not correlate well with the ammonia scavenging effect of the administered HPN-100.

If the 19 g dose of HPN-100 is determined to be inadequate (e.g. patient requires an increase in dietary protein which would result in excretion of waste nitrogen exceeding his or her urea synthesis capacity and PAGN excretion), HPN-100 dose would be increased sufficiently to cover the necessary dietary protein and the same methodology of dose adjustment based on urinary PAGN excretion would be applied to determine that dosage of HPN-100.

In a subject having little or no urea synthesis capacity where essentially all urinary nitrogen would be accounted for by PAGN, the ammonia scavenging effect may be monitored by determination of total urinary nitrogen (TUN), rather than directly measuring PAGN levels in the urine.

Optionally, the TUN can be used as a measure of urea synthesis capacity, by subtracting the amount of nitrogen present as PAGN.

Example 10

Determination of a Dosage of HPN-100 for a Patient Already on Sodium PBA

A patient with a UCD already on sodium PBA who is to be transitioned to HPN-100 would undergo assessment of dietary protein and measurement of urinary PAGN excretion.

If the patient is judged to be adequately controlled on sodium PBA, then the starting dose of HPN-100 would be the amount necessary to deliver the same amount of PAA (e.g. 19 grams of HPN-100 would correspond to 20 grams of sodium PBA). Subsequent dose adjustment would be based on repeated measurement of urinary PAGN as well as assessment of dietary protein and ammonia. However, as demonstrated by the observations described herein, the physician would not use plasma levels of PAA or PBA either to determine the initial dosage of HPN-100 or adjust the dosage of HPN-100 or otherwise guide treatment, as those levels do not correlate well with the ammonia scavenging effect of the administered HPN-100.

If the patient is determined to be inadequately controlled on sodium PBA, then the starting dose of HPN-100 would be selected to deliver an amount of PAA higher than the dose of sodium PBA provided such HPN-100 dosage is otherwise appropriate. Subsequent dose adjustment would be based on repeated measurement of urinary PAGN as well as assessment of dietary protein and plasma ammonia. However, as demonstrated by the observations described herein, the physician would not use plasma levels of PAA or PBA either to determine the initial dosage of HPN-100 or adjust the dosage of HPN-100 or otherwise guide treatment, as those levels do not correlate well with the ammonia scavenging effect of the administered HPN-100.

Optionally, for example in a 'fragile' UCD patient with a history of repeated episodes of hyperammonemia, the conversion from sodium PBA to HPN-100 might occur in more than one step, whereby, at each step, the dose of sodium PBA would be reduced in an amount corresponding to the amount of PAA delivered by the incremental dose of HPN-100.

If the dose of HPN-100 is determined to be inadequate (e.g. patient requires an increase in dietary protein which would result in production of waste nitrogen exceeding his or her urea synthesis capacity and PAGN excretion), HPN-100 dose would be increased sufficiently to cover the necessary dietary protein and the same methodology of dose adjustment based on urinary PAGN excretion would be applied.

The examples set forth herein are illustrative only, and should not be viewed as limiting the invention.

The invention claimed is:

1. A method of treating a patient having a urea cycle disorder comprising (a) determining a target urinary phenylacetyl glutamine (PAGN) output (b) calculating an effective initial dosage of a phenylacetic acid (PAA) prodrug selected from glyceryl tri-[4-phenylbutyrate] (HPN-100) and phenylbutyric acid (PBA) or a pharmaceutically acceptable salt of PBA, wherein the effective dosage of PAA prodrug is calculated based on a mean conversion of PAA prodrug to urinary PAGN of about 60%; and (c) administering the effective initial dosage of PAA prodrug to the patient.

2. The method of claim **1**, wherein target urinary PAGN output is determined as a ratio of the concentration of urinary PAGN to urinary creatinine.

3. The method of claim **1**, wherein administration of the effective initial dosage of PAA prodrug produces a normal plasma ammonia level in the patient.

4. The method of claim **1**, wherein the target PAGN output takes into account the patient's dietary protein intake.

5. The method of claim **1**, wherein the target PAGN output takes into account the patient's residual urea synthesis capacity.

6. The method of claim **1**, wherein the PAA prodrug is HPN-100.

7. The method of claim **1**, wherein the pharmaceutically acceptable salt of PBA is sodium PBA.

8. A method of administering a phenylacetic acid (PAA) prodrug selected from glyceryl tri-[4-phenylbutyrate] (HPN-100) and phenylbutyric acid (PBA) or a pharmaceutically acceptable salt of PBA to a patient having a from urea cycle disorder comprising (a) administering a first dosage of the PAA prodrug; (b) determining urinary phenylacetyl glutamine (PAGN) excretion following administration of the first dosage of the PAA prodrug; (c) determining an effective dosage of the PAA prodrug based on the urinary PAGN excretion, wherein the effective dosage is based on a mean conversion of PAA prodrug to urinary PAGN of about 60%; and (d) administering the effective dosage to the patient.

9. The method of claim **8**, wherein urinary PAGN excretion is determined as a ratio of the concentration of urinary PAGN to urinary creatinine.

10. The method of claim **8**, wherein the pharmaceutically acceptable salt of PBA is sodium PBA.

11. The method of claim **8**, wherein the PAA prodrug is HPN-100.

12. The method of claim **8**, wherein administration of the effective dosage of PAA prodrug produces a normal plasma ammonia level in the patient.

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